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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,203	03/21/2007	Kausik Si	68103-PCT-US/JPW/CH	5211

23432 7590 10/05/2011

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	PAPER NUMBER
1636	
MAIL DATE	DELIVERY MODE
10/05/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,203	SI ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-16 and 25-28* is/are pending in the application.

5a) Of the above claim(s) *14-16* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-13 and 25-28* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☒ The specification is objected to by the Examiner.

11)☒ The drawing(s) filed on *04 May 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/4/2006; 3/27/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 5/4/2006, in which claims 17-24 and 29-43 were canceled. Receipt is also acknowledged of an amendment, filed 4/29/2010, in which claims 2 and 15 were amended. Claims 1-16 and 25-28 are pending.

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 7/27/2011 is acknowledged.

Claims 14-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/27/2011.

An examination on the merits of claims 1-13 and 25-28 follows.

Information Disclosure Statement

Receipt of information disclosure statements, filed on 5/4/2006 and 3/27/2007, is acknowledged. The signed and initialed PTO 1449s have been mailed with this action.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c). See the citizenship, residence and post office address of Kausik Si.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below.

For example, Fig. 3A, Fig. 7A, page 14, line 6, page 27, line 7, 28 and 34, and page 32, line 7 contain sequences that are not referred to by the use of a sequence identifier. Where the description or claims of a patent application discuss a sequence that is set forth in the Sequence Listing, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

In response to this office action, Applicant must comply with the sequence rules, 37 CFR 1.821 - 1.825. The nature of the non-compliance did not preclude an examination of the elected invention on the merits, the results of which are presented below.

Drawings

The drawings are objected to because part D of Fig. 7 is not labeled in the drawing. The specification describes Figure 7D at page 14; however, the figure does not contain a panel labeled "D." Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement

drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

The disclosure is objected to because of the following informalities:

1. The description of Fig. 12 refers to "top" rather than "A" and "below the schematic" rather than "B." See the paragraph bridging pages 17-18.

2. At page 28, line 1, the word "mMESSAGE" is misspelled.

Appropriate correction is required.

The use of the trademark TRIZOL (page 26, lines 7 and 29), MMESSAGE MMACHINE (page 28, line 1), and IPGPHOR (page 28, line 13) has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 and 25-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for carrying out the claimed methods with the prior art *Aplysia californica* CPEB protein taught by Liu et al (Brain Research, Vol. 959, pages 68-76, January 2003, cited as reference 3 on the IDS filed 5/4/2006), does not reasonably provide enablement for using any other CPEB protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: Claims 1-13 are drawn to a method, which encompasses the steps of (a) contacting a population of cells with an agent, each of which cells comprises (i) an expressible nucleic acid comprising a sequence encoding a reporter protein that is translationally repressed by a cytoplasmic polyadenylation element (CPE) and (ii) a cytoplasmic polyadenylation element binding (CPEB) protein in its non-prion form; and (b) determining whether the amount of reporter protein expressed in the presence of the agent is greater than the amount of reporter protein expressed in the absence of the agent, whereby greater reporter protein expression in the presence of the agent indicates that the agent facilitates the conversion of a CPEB protein from its non-prion form to its prion form. The nature of the invention is complex in that in that the CPEB protein must be capable of adopting a prion form. Furthermore, the nature of the invention is complex one must be capable of using the CPEB protein to bind to the CPE to repress production of the reporter protein.

Claims 25-28 are drawn to a method, which encompasses the steps of (a) contacting a population of CPEB protein with an agent, wherein a predetermined portion of the CPEB protein population is in its non-prion form; and (b) determining whether the portion of the CPEB protein population in its prion form is greater in the presence of the agent than in the absence of the agent. Dependent claim 28 limits the determining step to determining the ability of CPEB protein to increase the expression of a protein that is translationally repressed by a CPE. The nature of the invention is complex in that in that the CPEB protein must be capable of adopting a prion form. Furthermore, the nature of the invention is complex one must be capable of using the CPEB protein to bind to the CPE to repress production of the reporter protein.

Breadth of the claims: The claims are broadly drawn to methods that require any CPEB protein to be capable of converting from a non-prion form to a prion form. The CPEB protein may be from any isoform from any species of organism. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims.

Guidance of the specification and existence of working examples: The specification defines the term "prion" form of CPEB to mean the form of CPEB protein which exists in a self-perpetuating and active state (page 20, lines 24-26). The specification defines the term "non-prion" form of CPEB protein to mean the form of CPEB protein, which, although having the same amino acid sequence of the prion form, exists in a non-self-perpetuating and non-active state (page 20, lines 26-28). Thus, the "prion" form is a form that has undergone a conformational change relative to the non-prion form (e.g., page 1, lines 15-27).

The specification teaches that CPEB was initially identified in *Xenopus* oocytes as a translational regulator that activates dormant mRNAs by elongating their poly(A) tails (e.g., page 2, lines 23-25). In some cases, CPEB can also act as a repressor, and the switch from activator to repressor is controlled by phosphorylation (e.g., page 2, lines 25-28). The specification teaches that CPEB is involved in the activation of translationally dormant mRNAs, where CPEB is activated and then catalyzes the polyadenylation of specific mRNAs, which in turn promotes their translation (e.g., page 5, line 24 to page 6, line 5).

The working examples are directed to a neuron-specific form of CPEB in an unnamed *Aplysia* species, where the protein is referred to as ApCPEB (e.g., page 25, lines 10-11). The specification teaches that protein synthesis of ApCPEB is induced by serotonin, and depletion of ApCPEB locally at the activated synapse inhibits the long-term maintenance of synaptic

facilitation but not its early expression at 24 hrs. (e.g., page 25, lines 10-20; page 39, line 13 to page 40, line 22; page 41, line 19 to page 42, line 34; page 44, line 3 to page 46, line 6; Figs. 1-2, 4 and 6). The specification asserts that similar isoforms have been identified in *Drosophila*, mouse and human nervous system, suggesting that the mechanism of serotonin induction and results of depletion are evolutionarily conserved (e.g., page 25, lines 22-25). The *Drosophila* protein is referred to as CG5735 (e.g., page 29, lines 19-24; page 38, lines 11-22). CG5735 is expressed in the larval stages and adult tissues, including adult brain (e.g., page 38, lines 11-22). The human protein is referred to as KIAA0940 (e.g., page 50, lines 16-17). The specification teaches that the N-terminal region of ApCPEB has the features of a prion determinant in that it has an unusually high content of the amino acids glutamine and asparagine (Q+N) and lacks predictable secondary structure (e.g., page 50, lines 1-11). Specifically, the N-terminal 160 amino acids of ApCPEB have a Q+N content of 48% (e.g., page 50, lines 5-9; Fig. 7A). The specification teaches that CG5735 alt1 has a Q+N content of 35% for its N-terminal 82 amino acids, and KIAA0940 has 18% Q+N content for its N-terminal 205 amino acids (e.g., page 50, lines 15-18). A Q+N content of 10% is typical of proteins that do not adopt a prion conformation (e.g., page 50, lines 6-8). Further, the specification teaches that CG5735 and KIAA0940 do not have predictable secondary structure (e.g., page 50, lines 118-20). The specification provides experimental evidence to demonstrate that ApCPEB adopts a prion conformation, which is the active form of the protein capable of binding a CPE (e.g., pages 50-62). No working examples are provided that demonstrate that any other CPEB proteins are capable of adopting a prion form. No evidence is provided that *Drosophila* CG5735 or human KIAA0940 adopt a prion form. Furthermore, no evidence is provided that CPEB proteins other

than ApCPEB bind a CPE in the prion form. No evidence is provided that *Drosophila* CG5735 or human KIAA0940 bind a CPE.

Predictability and state of the art: The prior art teaches that the *Aplysia* genus is comprised of some 35 species grouped into 5 distinct subgenera (Nambu et al. The Journal of Neuroscience, vol. 6, No. 7, pages 2026-2036, July 1996; e.g., page 2026, right column, last paragraph; Table 1). Nambu et al teach that the *Aplysia* species have varying numbers of gene copies with a gene family and varying percent sequence homology for paralogs across the different species (e.g., Abstract; page 2033, right column). Liu et al (Brain Research, Vol. 959, pages 68-76, January 2003, cited as reference 3 on the IDS filed 5/4/2006) teach the amino acid sequence of a nervous tissue isoform of CPEB of *Aplysia californica* (e.g.,ApCPEB77 of Fig. 4). The sequence of Liu et al contains the Q+N regions described in the present specification. Thus, given the disclosure of a single *Aplysia* sequence in the prior art and unpredictable variability in the gene sequence across species, one would not know how to make CPEB sequences representative of the entire *Aplysia* genus.

Liu et al (Brain Research, Vol. 959, pages 68-76, January 2003, cited as reference 3 on the IDS filed 5/4/2006) teach that the N-terminal sequences of ApCPEBs show little similarity to CPEBs of other animals (e.g., paragraph bridging pages 72-73). Darnell et al (Cell, Vol. 115, pages 767-770, December 2003, cited as reference 4 on the IDS filed 5/4/2006) discuss the work of Si et al and state, "Relating the current work to mammalian neurons will require establishing a clearer relationship between the ApCPEB and mammalian isoforms of CPEB." See page 768, left column, full paragraph. Darnell et al note that Si et al disclose that the N-terminus of ApCPEB is necessary and sufficient to act as a prion-like domain, and this region is 160 amino

acids in length with 50% Q/N content (e.g., page 767, Right column, 2nd full paragraph). Such Q/N-rich regions of mammalian isoforms were not known in the art. Darnell provides a single example of a brain specific isoform in mice (mCPEB-3), which differs from other mammalian isoforms in that it has a Q-rich domain in the first 30 amino acids (e.g., page 768, left column, full paragraph). However, the mCPEB-3 protein has only 10% Q+N over the next 130 amino acids, which does not represent an elevated level of Q+N (e.g., page 768, left column, full paragraph). The post filing art also notes that the degree of poly Q conservation in CPEB across phyla is not dramatic (Richter, JD. TRENDS in Biochemical Sciences, Vol. 32, No. 6, pages 279-285, May 2007). Richter teaches that CPEB2 is the most Q-rich of the CPEB proteins in mammals, yet it has a stretch of only 12 residues out of 40 that are Q (e.g., paragraph bridging pages 283-284). Thus, mammalian CPEB proteins do not contain a domain that would necessarily and predictably adopt a prion form (e.g., Darnell et al. page 768, left column, full paragraph; Richter, JD. paragraph bridging pages 283-284). Furthermore Kurihara et al (Biology of Reproduction, Vol. 69, pages 261-268, April 2003) teach that the precise functions of KIAA0940 of human and mouse are unknown, and sequence data is only available for human KIAA0940 (e.g., page 261, right column, 2nd full paragraph; Fig. 1). Moreover, CPEB2 and CPEB3 do not bind to a cytoplasmic polyadenylation element (Huang et al. The EMBO Journal, Vol. 25, pages 4865-4876, October 2006; e.g., Abstract; paragraph bridging pages 4865-4866).

Amount of experimentation necessary: Further experimentation would be required to identify CPEB proteins that have a Q/N-rich region. Once such variants are identified, one would be required to experimentally test such variants for the ability to adopt a prion form. Next

one would be required to test for the ability of the CPEB protein to bind a cytoplasmic polyadenylation element (CPE).

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. Therefore, claims 1-13 and 25-28 are not considered to be fully enabled by the instant specification.

Claims 1-13 and 25-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims encompass the provision of a genus of cytoplasmic polyadenylation element binding (CPEB) proteins that function to adopt a prion form and bind a cytoplasmic polyadenylation element (CPE).

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof.

The specification defines the term "prion" form of CPEB to mean the form of CPEB protein which exists in a self-perpetuating and active state (page 20, lines 24-26). The

specification defines the term "non-prion" form of CPEB protein to mean the form of CPEB protein, which, although having the same amino acid sequence of the prion form, exists in a non-self-perpetuating and non-active state (page 20, lines 26-28). Thus, the "prion" form is a form that has undergone a conformational change relative to the non-prion form (e.g., page 1, lines 15-27).

The working examples are directed to a neuron-specific form of CPEB in an unnamed *Aplysia* species, where the protein is referred to as ApCPEB (e.g., page 25, lines 10-11). The specification teaches that protein synthesis of ApCPEB is induced by serotonin, and depletion of ApCPEB locally at the activated synapse inhibits the long-term maintenance of synaptic facilitation but not its early expression at 24 hrs. (e.g., page 25, lines 10-20; page 39, line 13 to page 40, line 22; page 41, line 19 to page 42, line 34; page 44, line 3 to page 46, line 6; Figs. 1-2, 4 and 6). The specification asserts that similar isoforms have been identified in *Drosophila*, mouse and human nervous system, suggesting that the mechanism of serotonin induction and results of depletion are evolutionarily conserved (e.g., page 25, lines 22-25). The *Drosophila* protein is referred to as CG5735 (e.g., page 29, lines 19-24; page 38, lines 11-22). CG5735 is expressed in the larval stages and adult tissues, including adult brain (e.g., page 38, lines 11-22). The human protein is referred to as KIAA0940 (e.g., page 50, lines 16-17). The specification teaches that the N-terminal region of ApCPEB has the features of a prion determinant in that it has an unusually high content of the amino acids glutamine and asparagine (Q+N) and lacks predictable secondary structure (e.g., page 50, lines 1-11). Specifically, the N-terminal 160 amino acids of ApCPEB have a Q+N content of 48% (e.g., page 50, lines 5-9; Fig. 7A). The specification teaches that CG5735 alt1 has a Q+N content of 35% for its N-terminal 82 amino

acids, and KIAA0940 has 18% Q+N content for its N-terminal 205 amino acids (e.g., page 50, lines 15-18). A Q+N content of 10% is typical of proteins that do not adopt a prion conformation (e.g., page 50, lines 6-8). Further, the specification teaches that CG5735 and KIAA0940 do not have predictable secondary structure (e.g., page 50, lines 118-20). The specification provides experimental evidence to demonstrate that ApCPEB adopts a prion conformation, which is the active form of the protein capable of binding a CPE (e.g., pages 50-62). No working examples are provided that demonstrate that any other CPEB proteins are capable of adopting a prion form. No evidence is provided that *Drosophila* CG5735 or human KIAA0940 adopt a prion form. Furthermore, no evidence is provided that CPEB proteins other than ApCPEB bind a CPE in the prion form. No evidence is provided that *Drosophila* CG5735 or human KIAA0940 bind a CPE.

The prior art teaches that the *Aplysia* genus is comprised of some 35 species grouped into 5 distinct subgenera (Nambu et al. The Journal of Neuroscience, vol. 6, No. 7, pages 2026-2036, July 1996; e.g., page 2026, right column, last paragraph; Table 1). Nambu et al teach that the *Aplysia* species have varying numbers of gene copies with a gene family and varying percent sequence homology for paralogs across the different species (e.g., Abstract; page 2033, right column). Liu et al (Brain Research, Vol. 959, pages 68-76, January 2003, cited as reference 3 on the IDS filed 5/4/2006) teach the amino acid sequence of a nervous tissue isoform of CPEB of *Aplysia californica* (e.g.,ApCPEB77 of Fig. 4). The sequence of Liu et al contains the Q+N regions described in the present specification. Thus, given the disclosure of a single *Aplysia* sequence in the prior art, Applicant was not in possession of a genus of *Aplysia* CPEB sequences that have the claimed functions.

Liu et al (Brain Research, Vol. 959, pages 68-76, January 2003, cited as reference 3 on the IDS filed 5/4/2006) teach that the N-terminal sequences of ApCPEBs show little similarity to CPEBs of other animals (e.g., paragraph bridging pages 72-73). Darnell et al (Cell, Vol. 115, pages 767-770, December 2003, cited as reference 4 on the IDS filed 5/4/2006) discuss the work of Si et al and state, "Relating the current work to mammalian neurons will require establishing a clearer relationship between the ApCPEB and mammalian isoforms of CPEB." See page 768, left column, full paragraph. Darnell et al note that Si et al disclose that the N-terminus of ApCPEB is necessary and sufficient to act as a prion-like domain, and this region is 160 amino acids in length with 50% Q/N content (e.g., page 767, Right column, 2nd full paragraph). Such Q/N-rich regions of mammalian isoforms were not known in the art. Darnell provides a single example of a brain specific isoform in mice (mCPEB-3), which differs from other mammalian isoforms in that it has a Q-rich domain in the first 30 amino acids (e.g., page 768, left column, full paragraph). However, the mCPEB-3 protein has only 10% Q+N over the next 130 amino acids, which does not represent an elevated level of Q+N (e.g., page 768, left column, full paragraph). The post filing art also notes that the degree of poly Q conservation in CPEB across phyla is not dramatic (Richter, JD. TRENDS in Biochemical Sciences, Vol. 32, No. 6, pages 279-285, May 2007). Richter teaches that CPEB2 is the most Q-rich of the CPEB proteins in mammals, yet it has a stretch of only 12 residues out of 40 that are Q (e.g., paragraph bridging pages 283-284). Thus, mammalian CPEB proteins do not contain a domain that would necessarily and predictably adopt a prion form (e.g., Darnell et al. page 768, left column, full paragraph; Richter, JD. paragraph bridging pages 283-284). Furthermore Kurihara et al (Biology of Reproduction, Vol. 69, pages 261-268, April 2003) teach that the precise functions

of KIAA0940 of human and mouse are unknown, and sequence data is only available for human KIAA0940 (e.g., page 261, right column, 2nd full paragraph; Fig. 1). Moreover, CPEB2 and CPEB3 do not bind to a cytoplasmic polyadenylation element (Huang et al. The EMBO Journal, Vol. 25, pages 4865-4876, October 2006; e.g., Abstract; paragraph bridging pages 4865-4866). Thus, one would have recognized that Applicant was not in possession of CPEB proteins with the claimed functions, where the proteins are obtained from species other than *Aplysia californica* as disclosed by Liu et al.

The results of protein sequence comparisons are not necessarily predictive of the ability of the protein to adopt a prion form and to bind to a CPE. Thus, it is impossible for one to extrapolate from the *Aplysia californica* sequence disclosed by Liu et al, those proteins that would necessarily meet the structural/functional characteristics of the rejected claims.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of CPEB proteins, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The

compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In the instant case, the prior art provides only the *Aplysia californica* sequence.

Given the very large genus of CPEB proteins encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to the ability of known CPEB proteins to adopt a prion form and bind a CPE, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus. There is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those proteins that satisfy the functional limitations of the claims with regard to the ability of the protein to adopt a prion form, because the art questions whether the level of Q+N in known proteins is sufficient to confer the prion conformation and no experimental evidence of prion formation has been provided by the prior art or present specification. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 1-13 and 25-28.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is (571)272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Art Unit 1636